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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/683,753	10/13/2003	Richard P. Haugland		5050

23358 7590 10/02/2006

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EXAMINER
FREDMAN, JEFFREY NORMAN

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 10/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	**Application No.** 10/683,753	**Applicant(s)** HAUGLAND ET AL.	
	Examiner Jeffrey Fredman	**Art Unit** 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *44* is/are allowed.

6)☒ Claim(s) *1-43* is/are rejected.

7)☒ Claim(s) *7,8,18,19 and 26-37* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

1. The objection to claims 1, 13 and 25 is withdrawn in view of the amendment.

Claim Rejections - 35 USC § 112

2. Claims 1-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1, 13, 25, the amendment to the R^2 group renders the claim indefinite because the phrase "TAIL is a heteroatom-containing moiety" is not linked to any element. That is, R2 can no long be a "TAIL" since that element was deleted and therefore the phrase regarding the TAIL lacks antecedent basis.

Claim Rejections - 35 USC § 102

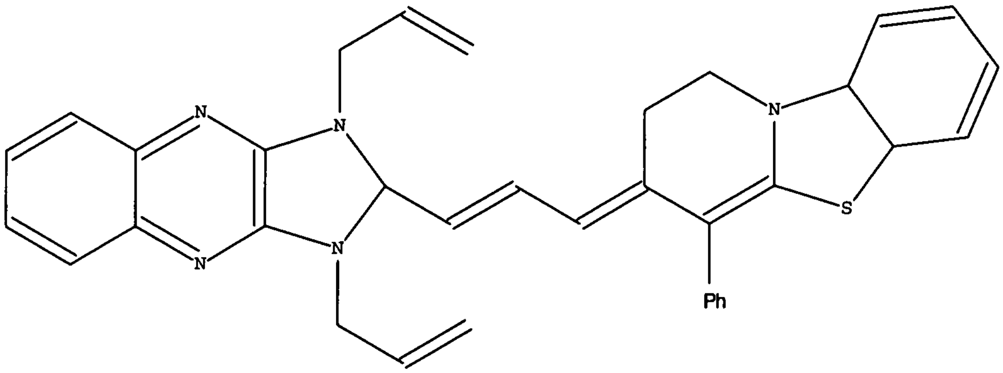
3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-4, 13 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Haseltine et al (U.S. Patent 4,003,750).

Heseltine teaches a method of claims 1 and 13 for determining the presence of an analyte comprising:

(a) combining said sample with a staining solution wherein said staining solution (see column 18, lines 20-67, which teaches mixing the dyes with gelatin (see column 18, line 21) and determining whether the dyes function as sensitizers) where the compound below is comprises a dye compound having the formula:



(see column 12, example 3, lines 55-end).

This compound meets the claim, since there is an A, which represents the atoms necessary to form two fused aromatic rings having 6 atoms in each ring wherein some of the ring atoms are nitrogen,

Where X is selected from the group consisting of NR^{15}, with R^{15} being an alkyl group with three carbons,

Where all beta is 0 and alpha is 1 so that alpha + beta = 1,

Where R2 is an alkyl group having three carbons,

Where n= 1,

Where Y is C=C and m+p = 1

And where the remaining substitutents permit the presence of the cyclic substituents and the aromatic ring. In particular, R3, R4, R5 and R6 are all indicated as being permissive of having a cyclic substituent which may have 1-6 carbons, as well as various alkyl groups which may have 1-6 carbons, which may be substituted.

(b) incubating said sample and said staining solution for a sufficient amount of time to form a dye analyte complex (see column 18, example 16, where Heseltine teaches methods of incubating samples and dyes to form a complex),

(c) illuminating said complex with an appropriate wavelength whereby the presence of said analyte is determined (see example 16, lines 25-30, where a Tungsten light is used to illuminate the samples and determine the functionality of the sensitizing dyes).

With regard to claim 2, 14, Heseltine teaches the presence of gelatin in the emulsion (see column 18, lines 21-22, where gelatin is a poly amino acid and where gelatin is relatively neutral).

With regard to claims 3-4, Heseltine teaches placement on a solid matrix which is a polymeric gel (see column 18, lines 25-28, where the support is a cellulose acetate film support that is polymeric).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

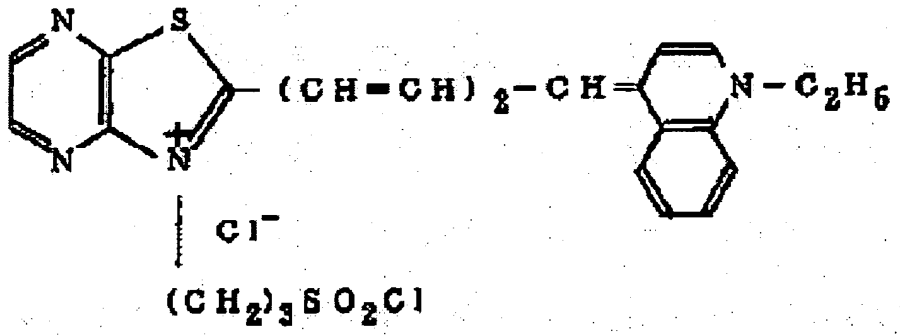
6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-4, 6, 9, 10, 13-17, 20, 21, 23-25, 38, 39 and 41-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katayose et al (JP 05-287209).

Attached is a translation of the detailed description of the Katayose patent. The rejection will refer to the paragraph number of the Japanese patent and to the page number of the translation).

> Katayose teaches a method of claims 1 and 25 for determining the presence of an nucleic acid analyte in a sample (see page 30, lines 1-35, for example) comprising:
>
> (a) combining said sample with a staining solution wherein said staining solution (see paragraph 0026, 0029, pages 8-9 of translation, which teaches detection of nucleic acid by sequencing and binding of the dye to the primer) where the compound below is comprises a dye compound having the formula:



(see paragraph 0020, page 7 of translation).

This compound meets the claim, since there is an A, which represents the atoms necessary to form one fused aromatic ring having 6 atoms in each ring wherein some of the ring atoms are nitrogen,

Where X is S,

Where n is 2,

Where R2 is an alkyl group having three carbons,

Where Y is C=C and m+p = 1

Where R5 is an alkyl group,

Where R30, R31 and R32 are H,

And where the remaining substitutents permit the presence of the cyclic substituents and the aromatic ring. In particular, R3, R4, R6 and R7 are all indicated as being permissive of having a cyclic substituent which may have 1-6 carbons, as well as various alkyl groups which may have 1-6 carbons, which may be substituted.

(b) incubating said sample and said staining solution for a sufficient amount of time to form a dye analyte complex (see paragraph 0026, page 8 of the translation, where Katayose teaches a method of forming a covalent bond between the dyes and oligonucleotide primers),

(c) illuminating said complex with an appropriate wavelength whereby the presence of said analyte is determined (see paragraph 0029, page 9 of the translation, where Katayose teaches measurement of the dye using a laser with a wavelength of 780nm).

With regard to claim 2, Katayose teaches detection of nucleic acid (see paragraph 0029, page 9 of the translation, where Katayose teaches nucleic acid detection).

With regard to claims 3-4, 9, 10, 20, 21, 23, 24, 38, 39, 41-43, Katayose teaches detection on a sequencing gel with electrophoretic separation (see paragraph 0029, page 9 of the translation, where Katayose teaches nucleic acid detection on a sequencing gel and where the nucleic acid is a "portion" of a cell but is free from cells as it has been purified).

With regard to claims 6, 17, Katayose teaches heating the oligonucleotide primer and the labeling dye together (see paragraph 0026, page 8 of translation).

With regard to claims 13-14, Katayose suggests detection of proteins which includes neutral proteins (see paragraph 0015, page 5 of translation).

With regard to claim 15, Katayose teaches a dye where R2 is a C2 alkyl group substituted with S.

With regard to claim 16, Katayose teaches a fused aromatic ring of R6 and R7.

Katayose does not teach the use of formula 15 in the sequencing method of the example.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the compound of formula 15 in the sequencing method since Katayose teaches this express fluorescent dye and teaches that these fluorescent dyes can be used in sequncing reactions (see paragraph 0029, page 9 of the translation). An ordinary practitioner, given the short list of synthesized lables of Katayose, would have been motivated to use all of them in the sequencing example, including the compound of formula 15.

8. Claims 5, 11, 22 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katayose et al (JP 05-287209) in view of Mills et al (U.S. Patent 5,221,518).

Katayose teaches the limitations of claims 1-4, 6, 9, 10, 13-17, 20, 21, 23-25, 38, 39 and 41-43 as discussed above. Katayose does not expressly teach the type of gel used and does not teach agarose or polyacrylamide gels for sequencing or detection.

Mills teaches separation of sequencing reaction products using agarose or polyacrylamide gels (see column 21, lines 13-21).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use either agarose or polyacrylamide gels in sequencing as taught by Mills for the sequencing gels of Katayose since Mills notes

"The preferred method of separating the fragments is the standard procedure of agarose or polyacrylamide gel electrophoresis. Gels containing the appropriate amounts of agarose or polyacrylamide can be formulated for optimum separation of fragments in the 20 to 400 nucleotide range (see column 21, lines 13-21)." An ordinary practitioner would have been motivated to use agarose or polyacrylamide gels because these are preferred and are the standard procedures for separation of fragments in the 20-400 nucleotide range.

9. Claims 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Katayose et al (JP 05-287209) in view of Leushner et al (U.S. patent 6,083,699).

Katayose teaches the limitations of claims 1-4, 6, 9, 10, 13-17, 20, 21, 23-25, 38, 39 and 41-43 as discussed above. Katayose does not expressly teach in situ analysis.

Leushner teaches in situ sequencing (see column 8, lines 3-10).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the sequencing primer of Katayose in in situ sequencing since Leushner teaches "in-situ sequencing reactions to produce sequencing fragments within a histological specimen which are then removed from a selected location on the tissue preparation and loaded onto a gel for sequence analysis. This latter approach is particularly useful for evaluation of archived samples in retrospective studies where the outcome of a disease condition is known, but the potentially causative mutation is not (see column 8, lines 3-10)." An ordinary practitioner, motivated by Katayose to perform sequencing detection assays on samples, would have been further motivated to extend these assays to archived samples as taught by Leushner, in order to be able to perform retrospecitve studies on archival samples.

Allowable Subject Matter

10. Claims 7, 8, 18, 19 and 26-37 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims and if the 112, second paragraph rejection issue was corrected.

11. Claim 44 is allowed.

12. The elected compound is not taught or suggested by the prior art and would be allowable if presented in independent form.

13. The following is a statement of reasons for the indication of allowable subject matter: Claims 7, 8, 18 and 19 are drawn to methods in which biological membranes are removed and detergents are added. Claims 26-37 are drawn to subsitutions which are not taught or suggested by the prior art. Claim 44 incorporates the limitations of claims 7 and 8 and is therefore allowed.

Response to Arguments

14. Applicant's arguments filed September 11, 2006 have been fully considered but they are not persuasive.

Applicant argues that Haseltine requires a fused ring at position R^5 and that the current claims do not permit that sort of substitution. This is not correct because the current R^5 and R^6 may include a "cyclic substituent" which would certainly include a fused ring as one possible embodiment. There is nothing which distinguishes a "cyclic substituent" from a fused ring.

Applicant then argues that Haseltine does not teach the current method. In fact, given the broad scope of the claims, Haseltine anticipates the claimed method as discussed in the rejection. There is no limitation on the analyte of interest and silver pigment or the other dye in the composition could be the analyte as easily as anything else.

Applicant then argues that Katayose does not have a nitrogen in the ring. As shown in the structure in the rejection and in the reference, Katayose expressly teaches a compound with a nitrogen in that ring. Applicant's argument that the claims permit direct detection, rather than detection mediated by functionalization, is not persuasive since it does not reflect a limitation in the claims. There is no requirement in the claims that excludes nucleic acid linked dyes from forming the dye-analyte complex. Further, the covalent linkage to the nucleic acid may represent the formation of the dye-analyte complex itself. So Applicant appears to be arguing limitations not found in the claims.

With regard to the argument that R^2 excludes the Katayose reference, this argument fails on two grounds. First, the claim is indefinite given the "TAIL" phrase in the R^2 element and given this indefinitness, it is unclear if Katayose would apply on that ground. Second, the compound uses the open "comprising" language. This permits the inclusion of additional elements. In this case, R^2 has an alkyl chain in Katayose, along with the sulfonyl group and therefore, Katayose remains applicable on this ground as well.

Since the previous rejections are maintained, so are the additional 103 rejections, which are not separately argued.

Conclusion

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jeffrey Fredman
Primary Examiner
Art Unit 1637
9/27/05